Recent Progress in Human Epithelial Cell Culture System and Its Application to Canter Research

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Unlike in a conventional culture system, most somatic epithelial stem cells show higher telomerase activity and proliferate virtually infinitely in vivo. Therefore, if the in vivo niche for epithelial stem cells can be mimicked in vitro, it is possible to avoid cellular senescence. Indeed, recent progress in culture system indicates that at least several human epithelial cells can be infinitely propagated in culture. Liu et al. improved the culture system for keratinocytes with 3T3 feeder layer by adding ROCK inhibitor, Y-27632. Sato and Clevers established RSpondin-based 3D culture system in which LGR5-positive stem cells from multiple organs can form virtually ever-expanding epithelial organoids. These cells can be used as cells-of-origin for various cancers to make in vitro carcinogenesis models of a given cancer. These culture methods can be also used for establishment of not only normal human cells but also cancer cell lines. In this symposium, I would like to introduce recent advance of these culture methods and its application to establish ovarian cancer cell lines. We developed a novel culture method which can support proliferation of almost all primary epithelial ovarian cancer cells, as well as primary normal human oviductal epithelial cells. Cancer cells from fresh or frozen specimens were enriched by the anti-EpCAM antibody-conjugated magnetic beads, plated on Matrigel-coated plate and cultivated under the optimized culture conditions. Seventeen newly established ovarian cancer cell lines, which included all four major histotypes of ovarian cancer, were confirmed to express histotype-specific markers in vitro. Some of the cell lines from all the four histotypes, except mucinous type, generated tumors in immune-deficient mice and the xenograft tumor tissues recapitulated the corresponding original tissues faithfully. Furthermore, with poorly tumorigenic cell lines including mucinous type, we developed a novel xenograft model which could reconstruct the original tissue architecture through forced expression of a set of oncogenes followed by its silencing. With combination of the novel culture method and cell-derived xenograft system, virtually every epithelial ovarian cancer can be reconstituted in mice in a timely fashion.

[Honors, Committees and Public Service]

1998 Sugiura Award of the Japanese Society for Virology
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2010 Tamiya Award of Foundation for Promotion of Cancer Research
2017 Project Officer for eASIA.

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